Cerebral Blood Flow Tomography Using Technetium-99m-HMPAO

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d, l-hexamethyl-propyleneamine-oxim PAO forms a lipophilic complex with Technetium-99m, that diffuses freely across the blood: brain barrier. It was synthesized by R.D. Neirinckx and collaborators from Amersham International in England with the aim of developing a tracer for imaging cerebral blood flow CBF in man with gamma tomography (SPECT). PAO was chosen from a long series of lipophilic oxims because of its prolonged retention in the brain.

We have used PAO (also called "Ceretec") in more than 100 clinical studies. The aim was to examine the validity of the PAO tomograms as images of the distribution of CBF. As a standard of reference served CBF measurements based on the inhalation of Xenon-133, a technique based on the classical inert gas clearance principles. A brain dedicated, highly sensitive SPECT system, the TOMOMATIC 64, was used.

PAO was labelled with 0.5 to 1.0 GBq of Technetium-99m and the freshly prepared tracer was injected as an intravenous bolus. This bolus traverses the lung with an only 10% retention. Being carried to the brain, and to the other organs as well, in proportion to fractional blood flow the tracer diffuses out into the tissues. Here a rapid chemical conversion to a hydrophilic form occurs, so that about 50% of the amount delivered to the brain is retained: This retention is remarkably stable with a loss from the brain of only 0.5% per hour over the next 24 hours or longer.

The steady-state PAO tomograms taken after the first few minutes show a pattern that agree very closely to the Xenon-133 CBF tomograms. A simple algorithm correcting for the rapid but not instantaneous conversion (and fixation) was developed and using it the two techniques give virtually the same tomograms of CBF distribution. This was found to be the case in all clinical cases studied. In particular it was noted, that PAO does not show a delayed uptake in low flow regions with a damaged blood: brain barrier as seen with the I-123 labelled amines, that have been used for tomographic CBF studies.

As illustrated by clinical cases, PAO is the tracer of choice for many clinical purposes. In particular its use in the differentical diagnosis of dementia syndromes and in localizing epileptic foci deserves to be emphasized. PAO allows medium resolution tomograms (ca. 2.0 cm FWHM) to be obtained using a standard single-head rotating gamma camera and high resolution tomograms (0.8 to 1.0 cm FWHM) using a brain dedicated SPECT. The use of PAO in patients with cerebrovascular disease suffers from two limitations: a) the study can only be repeated after several hours

and b) one cannot measures absolute CBF values. These difficulties can be overcome by Xe-133. It, on the other hand, does not allow high image resolution.

The lecture ends by emphasizing the value of CBF tomography in the clinical routine: it gives direct information of an important functional parameter—the blood flow through the tissue—that cannot be imaged by the essentially structure-related CT or MR scanning techniques.

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Immunoscintigraphy (IS)

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IS belongs to the most important features of progress in nuclear medicine. Although preliminary attempts date back nearly 40 years ago the actual breakthrough was achieved by introducing radioactively labeled monoclonal antibodies (RAMAK) applied especially as "radioimmunococktails" (RIC) of a mixture of ¹³¹J-Anti-CEA** and ¹³¹J-Anti-CA-19-9** as first proposed by CHATAL et al in France and further promoted by our group in Federal Republic of Germany. ¹⁻⁴⁾ The following aspects are reviewed:

- 1. History based on the discoveries of EHRLICH, EDELMAN and PORTER, JERNE, MILSTEIN and KÖHLER, all honored by the NOBEL-PRICE.
 - 2. Radioactive Antibodies (RAB)

We used the above mentioned ¹³¹J-cocktail. The spectrum of previous and present RAB's is presented with detailed specifications on our RIC (Tables 1 and 2).

Some of our own experimental data are shown in Fig. 1.

3. Techniques

Planar (double radionuclide-double compound-isocontour-technique) and tomographic (SPECT) methods:

- A. SKELETAL IMAGING/URINARY BLADDER
 Tc-99m-HMDP 150-300 MBq i.v. RECORDING TIME: 5 MINUTES
- B. LIVER/SPLEEN/BONE MARROW
 Tc-99m-NANOCOLLOIDE 37-300 MBq i.v. RECORDING TIME: 3-5 MINUTES
- C. KIDNEY/URETER/URINARY BLADDER
 Tc-99m-DTPA 74-285 MBq i.v. RECORDING TIME: 3-5 MINUTES

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